

- Respiratory disease
  - Rheumatoid disease
  - Auto-immune disease
  - Allergy
  - Vascular disease
  - Skin disease
  - Gastrointestinal disease
  - Renal disease
  - Liver disease
  - Ocular disease
  - Ear disease
  - Neurological disease
  - Endocrine disease
  - Shock
  - Malignancy
  - Transplantation
  - Diabetes and obesity
- in a mammalian, including a human, subject.

*Rest.  
Electron  
Chain  
15-18*

*1/23*

14. A use according to claim 12 or 13 in which said ligand is {3,5-dibromo-4-[5-isopropyl-4-methoxy-2-(3-methyl-benzoyl-phenoxy)]phenyl}-acetic acid.

15. A method of screening for a dissociated glucocorticoid receptor (GR) antagonist comprising:

- a) contacting a candidate substance with a GR;
- b) determining binding of the candidate substance to the GR;
- c) selecting a candidate substance having binding affinity for the GR;
- d) determining activity of the selected candidate substance in GR-mediated transactivation of a glucocorticoid sensitive target gene;
- e) selecting a candidate substance having antagonist, but no agonist transactivation activity;

*N.A*

*antagonist - binds GR  
prevent binding of endogenous*

*agonist -*

- f) determining activity of the selected candidate substance in GR-mediated transrepression of a glucocorticoid sensitive target gene; and
- g) selecting the candidate substance having no antagonist transrepression activity.

16. A method according to claim 15 wherein the GR-mediated transactivation results in induction of tyrosine aminotransferase (TAT) in a rat hepatoma cell or in stimulation of MMTV (mouse mammary tumor virus) promoter in a HeLa cell.

17. A method according to claim 15 or 16 wherein the GR-mediated transrepression results in inhibition of a gene having pro-inflammatory or immuno-enhancing activity, such as a gene coding for a cytokine or an adhesion molecule or an enzyme each involved in inflammation or in a immune disorder including an auto-immune diseases.

*Cytokine  
adhesion molecule  
immune disorder*

18. A method according to claim 17 wherein the GR-mediated transrepression results in inhibition of TNF- $\alpha$ -induced activation of ICAM-1 promoter in a HeLa cell or in inhibition of LPS-induced production of IL-8 in a THP1-cell.

19. A method according to any one of claims 15 to 18 further comprising the step of testing the candidate substance *in vivo* by co-administering said substance with a glucocorticoid drug to a subject and determining the capability of the candidate substance to reduce a systemic side-effect of the glucocorticoid but retaining the anti-inflammatory activity of the glucocorticoid.

20. A method according to any one of claims 15 to 19 wherein said method is a high-throughput screening assay (HTS).

21. A method of treating a mammalian, including a human subject in the need thereof comprising the administration of a glucocorticoid receptor (GR)